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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,289	05/31/2002	Vega Masignani	PP01639.102; 2300-1639	6882

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
04/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,289	MASIGNANI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,24,26-28 and 30-36* is/are pending in the application.

4a) Of the above claim(s) *24 and 33-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 10, 26-28 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *091208*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendments filed 10/20/08 and 01/16/09 in response to the non-final Office Action mailed 05/20/08.

Status of Claims

2) Claim 1 has been amended via the amendment filed 01/16/09.

Claims 1, 10, 24, 26-28 and 30-36 are pending.

Claims 1, 10, 26-28 and 30-32 are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicant's Information Disclosure Statement filed 09/12/08. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Objection(s) Maintained

4) The objection to the specification made in paragraph 4 of the Office Action mailed 05/20/08 is maintained for the reasons set forth therein and herein below.

Applicants submit that none of the pending claims rely upon or refer to sequences in the cited PCT Application and therefore the sequences in the cited PCT Application are not essential. However, Applicants state that in order to facilitate prosecution of this case, they have filed a sequence listing which includes the same sequences as in the material incorporated by reference appended to the end of the sequence listing.

Applicants' arguments have been considered, but are not persuasive. The amino acid sequence of SEQ ID NO: 1331 that is recited in the instant claims and depicted on page 67 is the amino acids 959-976 of ORF 114-1 disclosed in WO 9936544. The claimed polypeptide that is 100 amino acids or less in length thus encompasses a fragment of ORF 114-1 disclosed in WO 9936544. Therefore, the pending claims do rely upon the partial sequence disclosed in WO 9936544. Applicants have not amended the disclosure to include the material incorporated by reference. No affidavit or declaration executed by the Applicant(s), or a practitioner representing

the Applicants(s), stating that the amendatory material consists of the same material incorporated by reference in the referencing application has been submitted. The objection stands.

Rejection(s) Withdrawn

5) The rejection of claims 1, 10, 26-28 and 30-32 made in paragraph 7 of the Office Action mailed 05/20/08 under 35 U.S.C § 112, first paragraph, as containing inadequate written description, is withdrawn in light of Applicants' amendment to the base claim. A new rejection is set forth below to address the claims as amended.

Applicants state that they have amended claim 1 to clarify that the amino acid sequence of SEQ ID NO: 1331 comprises the at least one antigenic determinant and can detect the presence of antibodies raised against *Neisseria meningitidis* serogroup B. Applicants submit that one of skill in the art would recognize that applicants had possession of SEQ ID NO: 1331 by virtue of disclosure of the structure thereof in the specification and therefore were in possession of the SEQ ID NO: 1331 which comprises the at least one antigenic determinant and can detect the presence of antibodies raised against any *Neisseria meningitidis* serogroup B. However, as explained under the rejection below, Applicants have not correlated the structure of one or more antigenic determinants within the 18 amino acid-long SEQ ID NO: 1331 with the requisite function, i.e., the capacity to detect the presence of antibodies raised against *Neisseria meningitidis* serogroup B. See the rejection set forth below.

New Rejection(s) Necessitated by Applicants' Amendment

Rejection(s) under 35 U.S.C § 112, First Paragraph (Written Description)

6) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7) Claims 1, 10, 26-28 and 30-32 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instantly recited SEQ ID NO: 1331 is 18 amino acids in length. The claimed purified polypeptide genus that comprises this 18 amino acid-long SEQ ID NO: 18 is 100 amino acids or less in length, or 50, 25 or 20 amino acids in length and comprises at least one antigenic determinant. The open claim language 'comprising' allows the claimed polypeptide to have any amino acids in any number and in any sequence along the length of SEQ ID NO: 1331 including those from non-meningococcal ORF 114-1 protein as long as the length of the polypeptide is 100 amino acids or less. The limitation '*N. meningitidis* serogroup B' encompasses any strain, any serotype, or any immunotype of *N. meningitidis* serogroup B. The limitation 'antibodies raised' includes monoclonal and polyclonal antibodies raised against any strain, any serotype, any subtype, or any immunotype of *N. meningitidis* serogroup B. Since the term 'at least' has no upper limit, the limitation 'at least one antigenic determinant' encompasses any number of antigenic determinants, all required to be comprised within the short peptide of SEQ ID NO: 1331 that is 18 amino acids in length. The limitation 'antigenic determinant' encompasses linear and conformational antigenic determinants or contiguous and discontiguous antigenic determinants. The amino acid sequence of SEQ ID NO: 1331 comprising at least one antigenic determinant is *required* to have the capacity to detect the presence of antibodies raised against *N. meningitidis* serogroup B. The specification intends at least diagnostic applications for the claimed polypeptide.

The written description requirement can be met by describing the claimed subject matter to a person skilled in the art using sufficiently detailed, relevant identifying characteristics such as functional characteristics, and correlating those functional characteristics with a disclosed structure. See *Enzo Biochem v. Gen-Probe,* 323 F.3d 956, 964, 967, 968 (Fed. Cir. 2002). Sufficient description to show possession of a genus may be achieved by means of disclosure of a representative number of polypeptides, defined by amino acid sequences falling within the scope of the genus, or recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may *not* be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

In the instant application, Applicants have shown possession of one peptide species, i.e., the full length SEQ ID NO 1331 that is 18 amino acids in length. The disclosed structure or the amino acid sequence of the peptide species, SEQ ID NO: 1331, is depicted on page 67 which is the amino acids 959-976 of ORF 114-1 disclosed in WO 9936544. This structure of SEQ ID NO: 1331 or the structure of one or more antigenic determinants comprised within the 18 amino acid-long SEQ ID NO: 1331 is not correlated with the *requisite* functional immunospecificity, i.e., the ability to detect the presence of antibodies raised against homologous or heterologous *N. meningitidis* serogroup B. The antibodies raised against homologous or heterologous *N. meningitidis* serogroup B are expected to be directed to surface-exposed antigenic determinants of a protein of said heterologous or homologous *N. meningitidis* serogroup B, but not to antigenic determinants of said protein that are non-surface-exposed or buried. Antibodies raised against a strain, serotype, subtype, or immunotype of *N. meningitidis* serogroup B are immunospecific to one or more surface-exposed strain-specific, serotype-specific, subtype-specific, or immunotype-specific antigenic determinants. However, the accessibility of SEQ ID NO: 1331 or at least one antigenic determinant therein, on the cell surface of any strain, serotype, subtype, or immunotype of *N. meningitidis* serogroup B is neither disclosed within the instant specification, nor is it known in the state of the art. It is well recognized in the art of meningococcal proteins that not all meningococcal proteins and not all parts of a particular meningococcal protein are exposed on the cell surface. See abstract of Gomez *et al. Vaccine* 14: 1340-1346, 1996; and Figure 4 of Malorny *et al. J. Bacteriol.* 180: 1323-1330, 1998, both of record. Some epitopes are buried while some are surface exposed. See abstract of Teerlink *et al. J. Exp. Med.* 166: 63-76, 1987 and Forest *et al. Gene* 192: 165-169, 1997, both of record. For instance, antibodies raised against the 13,000 Mr peptide CB1 could not be absorbed with intact outer membranes complexes suggesting that this peptide is buried within outer membranes of the bacteria. See abstract of Teerlink *et al.* Similarly, sera raised against certain epitopes of some meningococcal proteins failed to label whole cells suggesting lack of surface accessibility. See abstract of Ala'Aldeen *et al. Vaccine* 12: 535-541, 1994, of record. The state of the art recognizes that antibodies that react with intact meningococcal bacteria (and thereby detect the meningococcal bacteria) **must** recognize epitopes on the cell surface. See sentence bridging the two columns on page 1327 and page 1323 of Malorny *et al.* In the instant case, whether or not the at least one antigenic determinant of the 18

amino acid-long SEQ ID NO: 1331 is surface-exposed or buried deep within, is neither disclosed, nor is it known in the art. Whether or not the at least one antigenic determinant in SEQ ID NO: 1331 is serotype-specific or strain-specific is not known. There is inadequate written description establishing a structure-function relationship between the 18 amino acid-long SEQ ID NO: 1331, or at least one antigenic determinant therein, and its ability to detect the presence of antibodies raised against homologous or heterologous strain, serotype, subtype, or immunotype of *Neisseria meningitidis* serogroup B. Note that *Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111*, clearly states: 'Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed'. See page 1117. It should be noted that written description requires more than a mere statement that something is a part of the invention. Applicants have not described what contiguous or discontiguous antigenic determinants, or conformational or non-conformational epitopes of the claimed polypeptide comprising SEQ ID NO: 1331 are correlated with the required capacity to detect the presence of antibodies raised against any *Neisseria meningitidis* serogroup B. Applicants should note that written description requires more than a mere statement that something is part of the invention and a reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. The specific guidance, not general guidance is needed. A mere idea or unsubstantiated function is insufficient for written description; characterization of one or more *Neisseria meningitidis* serogroup B-specific antigenic determinants within the 18 amino acid-long SEQ ID NO: 1331 at a minimum are required.

With respect to the written description requirement, while 'examples explicitly covering the full scope of the claim language' typically will not be required, a sufficient number of representative species must be included 'to demonstrate that the patentee possesses the full scope of the [claimed] invention'. *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). In the instant case, Applicants' specification does not contain a written description sufficient to show that they had possession of the full scope of the claimed invention at the time the application was filed. The instant specification mentions of a peptide of SEQ ID NO: 1331 on page 67. However, the specification does not disclose a correlation between the requisite function (i.e., capacity to detect the presence of antibodies raised

against *Neisseria meningitidis* serogroup B) and the structure of at least one antigenic determinant within SEQ ID NO: 1331 responsible for that function, for one of skill in the art to know that Applicants were in possession of the claimed functional polypeptide. Clearly, Applicants did not describe the invention of the instant claims sufficiently to show that they had possession of the claimed genus of polypeptides. See e.g., *Noelle v. Lederman*, 355 F.3d 1343, 1348, 69 USPQ2d 1508, 1513 (Fed. Cir. 2004) ('invention is, for purposes of the written description inquiry, *whatever is now claimed*').

As known in the art of immunology, an epitope or antigenic determinant can be linear, or conformational or discontinuous, and it specifically interacts with its corresponding antibody based on the three dimensional structure of both the molecules and the fit between the molecules. See page 46 of Cruse *et al.*, *Illustrated Dictionary of Immunology*, 2nd Edn., CRC Press, 2003, of record. The specification does not adequately describe or identify the linear or conformational *Neisseria meningitidis* serogroup B epitopes that are serotype-specific, non-serotype-specific, or strain-specific, within the 18 amino acid-long SEQ ID NO: 1331. Discontiguous epitopes are formed from different regions of the primary sequence brought together by proper protein folding. Antibodies binding to conformational epitopes bind only to proteins folded into their proper native form. See page 166 of Cruse *et al. Illustrated Dictionary of Immunology*, 2nd Edn., CRC Press, 2003, of record. Linear epitopes are generally not found on the surface of a folded polypeptide and are available to antibodies only upon denaturation of a polypeptide. See page 382 of Cruse *et al*. Since the instant invention contemplates diagnostic applications for the claimed polypeptide, the claimed product has to detect raised antibodies having binding specificity to the properly folded polypeptide of SEQ ID NO: 1331 as found on the surface of any strain *Neisseria meningitidis* serogroup B. The structure of at least one antigenic determinant within the 18 amino acid-long SEQ ID NO: 1331 capable of detecting the presence of antibodies raised against any *Neisseria meningitidis* serogroup B is not described. This is important because whether or not SEQ ID NO: 1331 is present surface-exposed by every strain of *Neisseria meningitidis* serogroup B or a representative number of strains of *Neisseria meningitidis* serogroup B is not known. Furthermore, with specific regard to meningococcal proteins, it is known in the art that even the amino acid residues outside an antigenic determinant but in the vicinity of an antigenic determinant are critical to the immunospecific binding to

antibodies. For instance, McGuiness *et al.* (*Mol. Microbiol.* 7: 505-514, Feb 1993, of record) taught that "[a] single amino acid change within an epitope, or an amino acid deletion outside an epitope, were both associated with loss of subtype specificity resulting from a change in the predicted conformation at the apex of the loop structure" in case of a meningococcal polypeptide (see abstract). In the instant application, in addition to the lack of adequate description of the at least one antigenic determinant within SEQ ID NO: 1331 that has the capacity to detect antibodies raised against *Neisseria meningitidis* serogroup B, the precise amino acids outside the at least one antigenic determinant of the claimed polypeptide that may potentially influence the conformation and the antibody-detecting ability, is not described. The presence of one or more antigenic determinants within the short peptide of 18 amino acids, i.e., SEQ ID NO: 1331, which one or more antigenic determinants are *Neisseria meningitidis* serogroup B-specific, and therefore the diagnostic significance of the claimed polypeptide is purely speculative. Without a correlation between structure and function, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ….. does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is'). The instant claims are viewed as not meeting the written description provision of 35 U.S.C. § 112, first paragraph.

Remarks

8) Claims 1, 10, 26-28 and 30-32 stand rejected.

9) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

11) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

12) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

April, 2009